In re Application of: Dror OFER
Serial No.: 10/523,131
Filed: January 21, 2005
Final Office Action Mailing Date: July 21, 2009

Examiner: Borin, Michael L.
Group Art Unit: 1631
Attorney Docket: 35898
Confirmation No.: 1264

REMARKS

Reconsideration of the above-identified application in view of the amendments above and the remarks following is respectfully requested.

Claims 1-25, 29-57, 102, 103, 155-159 and 161-163 are in this Application. Claims 7, 10-13, 16-23, 37-39, 50-53, 57, 102, 103 and 157 have been withdrawn from consideration. Claims 1-4, 26, 29-33, 36, 41-46, 155, 156, 158, 159 and 161 have been rejected under 35 U.S.C. § 103. Claims 26-28, 58-101, 104-154, 160 and 164-171 have been canceled in a previous response. Claims 5, 155 and 156 have been canceled herewith. Claims 1, 2, 6-8, 11-13, 16, 24, 25, 34, 35, 44-49, 54-56 and 157 have been amended herewith.

Interview Summary

Applicant wishes to thank the Examiner for his attention and for his helpful suggestions during the telephone Interview held on October 13, 2009. In the Interview, Applicant reiterated the nature of the invention, differences from the prior art, and difficulties in claiming the complex subject of the invention. The Examiner explained the reasons for keeping the art rejection of record and invited Applicant to address the method of analysis in the claims. No agreement was reached during the Interview.

Amendments To The Claims

35 U.S.C. § 112, Second Paragraph, Rejections

The Examiner has stated that claims 1-6, 8, 9, 14, 15, 24-36, 40-49, 54-56, 155, 156 and 158-163 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Specifically, in one particular the Examiner has stated that it is not clear how *in vitro* assays will measure interaction with geometrical triangular structures used to describe the compounds in the assays, and that the relevance of claim limitations addressing "triangular geometric structures" and "triangle space", which are features of *in silico* modeling rather than *in vitro* testing, is not clear, as the active method step is performing *in vitro* assays.

Applicant has chosen to amend claim 1 so as to more clearly distinguish between the various components (e.g., *in silico* modeling and *in vitro* assaying) of the claimed method, and so as to clarify the meaning and role of terms such as "triangular geometric structures" and "triangle space". In addition, claim 1 has been amended so as to clarify the limitations on the recited method imposed by the claim recitations, and to better characterize the analysis component of the method, in accordance with the abovementioned Examiner's comments during the Interview.

Thus, claim 1 has been amended so as to recite:

"A method of obtaining information about a chemically active area of a target molecule, comprising:

(a) selecting a compound that is a substantially rigid chemical gauge comprising at least one set of three binding points in a substantially rigid triangular configuration, each of said at least one set of three binding points being selected capable of binding to a 3-point pharmacophore comprising a triplet of chemical binding points selected from the group consisting of acid, base, hydrophobic, hydrogen-bond donor, hydrogen-bond acceptor, and aromatic, wherein each pair of binding points of said 3-point pharmacophore is separated by a distance in a range of 2 to 12 angstrom;

(b) performing an assay for measuring an interaction of said target molecule with said gauge, thereby obtaining an assay result for said gauge;

(c) selecting additional substantially rigid chemical gauges according to said (a) so as to obtain a plurality of gauges, such that for a portion of

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triangle space comprising 50 % of said triangle space, said plurality of gauges is selected so as to comprise at least six gauges with a substantially rigid triangular configuration of binding points capable of chemically binding to each 3-point pharmacophore corresponding to a point in said portion of triangle space, wherein said triangle space defines all possible 3-point pharmacophores defined by a triplet of distances that form a triangle, each distance being in a range of 2-12 angstrom, and by a triplet of chemical binding point types for the triangle vertices, each chemical binding point type being selected from the group consisting of acid, base, hydrophobic, hydrogen-bond donor, hydrogen-bond acceptor, and aromatic;

(d) performing said (b) for each of said additional substantially rigid chemical gauges, so as to obtain a plurality of assay results; and

(e) identifying a plurality of spatially and chemically specific configurations of binding points in said chemically active area of said target molecule using a computational model in which said assay results represent interactions between configurations of binding points in said chemically active area and triangular geometric substructures, each triangular geometric substructure representing a set of three binding points of a gauge and being defined by a triplet of distances that form a triangle and by a triplet of chemical binding point types for the triangle vertices,

thereby obtaining information about said chemically active area."

Applicant believes that the above amendments clarify the subject matter by grouping selection of compounds ((a) and (c)), assaying ((b) and (d)) and analysis ((e)) in distinct paragraphs. Applicant further believes that the above amendments clarify the subject matter by describing selection and assaying for individual gauges ((a) and (b)).

Applicant contends that the amendments in (a), (b), (c) and (d) are purely cosmetic and do not affect the scope of the claim.

In addition, Applicant believes that the analysis of assay results as recited in (e) in claim 1 is sufficiently characterized to meet the Examiner's requests in this respect. The amendments in this respect are supported, for example, by claim 5.

As a result of the amendments to claim 1, claims 5, 155 and 156 have been canceled. Consequently, claims 6-8, 11-13, 16, 47-49 and 54-56 have been amended so as to depend from claim 1 instead of claim 5.

In addition, claims 24, 25, 34 and 35 have been amended so as to recite "plurality of gauges" instead of "set of gauges", in order to accord with the language of amended claim 1.

In addition, claim 157 has been amended so as to recite "identifying" instead of "analyzing", and "into account in said model" instead of "into account of said analyzing", in order to accord with the language of amended claim 1.

Applicant believes that amended claim 1 makes clear how "triangular geometrical substructures" are used in the recited computational model to represent the real-world compounds (gauges) for which *in vitro* assay results have been obtained. Thus, triangular geometrical substructures are not a feature of *in vitro* testing *per se*.

Applicant further believes that amended claim 1 makes clear that "triangle space" is a mathematical tool for defining all possible 3-point pharmacophores (within the range of parameters recited in claim 1), so as to precisely define the selection criteria for selecting gauges in order to obtain the recited plurality of gauges. Thus, the term "triangle space" is used to characterize the plurality of gauges selected for *in vitro* testing, and is not a feature of *in vitro* testing *per se*.

In another particular, the Examiner has stated that as claim 1 is amended to read on compounds comprising gauges, it is not clear whether the assaying is performed with compounds or with gauges, and it is not clear how an *in vitro* assay measures interaction with a geometrical feature of a compound.

As is made more clear in amended claim 1 above, there is no distinction between the recited gauge and the recited compound, as the term "gauge" is used to describe the recited compound. Thus, an assay performed for a gauge is an assay performed for a compound, not for a mere geometrical feature of a compound.

Applicant wishes to note that the term "gauge" is used thusly throughout the instant application.

In another particular, the Examiner has stated that claim 5 lacks antecedent basis, as claim 1 does not address a "target active area".

As discussed hereinabove, claim 5 has been canceled.

In another particular, the Examiner has stated that claims 44-49 are directed to binding of certain number of gauges and identifying certain amounts of different configurations, and that in the absence of further defining of the area to be assayed, it is not clear how one can know the amount of gauges that successfully bind to the target or the amount of different configurations to be discovered by the method prior to applying the method itself.

Claims 44-46 recite the use of successful binding of at least a minimal number (i.e., 60, 10 or 100) of distinct gauges.

Claims 47-49 recite identifying at least a minimal number (i.e., 40, 10 or 100) of configurations.

Applicant wishes to note that the method recited in claim 1 includes selecting additional gauges in order to obtain a plurality of gauges, and performing assays on the additional gauges in order to obtain a plurality of assay results. Applicant wishes to note further that the language of claim 1 does not exclude selecting some additional gauges after assay results for other gauges have already been obtained.

As would be apparent to one of ordinary skill in the art, one may readily select further gauges in order to obtain further assay results, to thereby obtain sufficient assay results such that the plurality of assay results includes at least the recited minimal number of successful binding results.

For example, gauges may be selected to have properties suitable for binding to the 3-point pharmacophores in the target, which result in a relatively high binding percentage to a target. Hence, it is likely that at least some of the gauges in the plurality of gauges will bind to the target. In contrast, sets of compounds described in the prior art comprise compounds suitable for binding only a small portion of available 3-point pharmacophores. Prior art compounds will likely exhibit a low probability of binding.

Similarly, as would be apparent to one of ordinary skill in the art, one may readily select further gauges in order to obtain further assay results, to thereby obtain sufficient assay results to enable the identifying of the recited minimal number of configurations.

It is well within the abilities of the skilled artisan to select additional gauges in a manner which provides the recited amount of gauges that successfully bind to the target and/or the amount of different configurations to be identified by the method.

Notwithstanding the above, Applicant has chosen to amend claims 44-46 in order to better characterize the limitations recited therein. Thus, claims 44-46 have been amended so as to recite "wherein said plurality of assay results comprises assay results showing successful binding of at least [60 or 10 or 100] distinct gauges".

The number of assay results sufficient to provide a given number (e.g., 100) of successful binding results for distinct gauges may be readily estimated for any given target based on the percentage of gauges which bind to the target, as determined, for example, by preliminary assay results. Thus, for example, for a target molecule which binds to at least 0.5 % of the gauges in a plurality of gauges (see for example, page 14, lines 16-18, of the instant application), approximately 20,000 gauges are sufficient to provide 100 successful binding results.

Applicant therefore believes to have overcome the Examiner's objections in this respect.

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35 U.S.C. § 112, First Paragraph, Rejections

The Examiner has stated that claims 1-6, 8, 9, 14, 15, 24-35, 40-49, 54-56, 155, 156 and 158-163 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention.

Specifically, in one particular the Examiner has stated that claim 1 introduces new matter by addressing "compounds comprising a set of ... gauges, each of said gauges comprising at least one set of three binding points", as the specification addresses chemical gauges and uses of libraries thereof in *in silico* methods, but does not address compounds as being comprised of a set of gauges.

As discussed hereinabove, the term "gauges", as used throughout the instant application, refers in general to compounds having the recited properties (e.g., rigidity, at least one set of three binding points) and not to components of such compounds or to mere *in silico* models of such compounds. Moreover, it is clear from the specification that such gauges are to be assayed *in vitro* in order to determine the interactions between the gauges and target, contrary to the Examiner's statement that only *in silico* uses of gauges are addressed by the specification. See for example, page 3, lines 4-14; page 28, lines 20-28; and page 29, line 18 to page 33, line 7, of the instant application.

In another particular, the Examiner has stated that claim 1 introduces new matter by addressing "analyzing said assay results using a plurality of said triangular geometric substructures", as the specification does not disclose using triangular geometric substructures to analyze *in vitro* assay results.

Contrary to the Examiner's statement, the analysis of assay results using triangular geometric substructures based on gauges is described, for example, on page 5, line 20, to page 6, line 1, of the instant application. Moreover, Applicant believes that it would be apparent to one of ordinary skill in the art that the "triangles"

repeatedly referred to in the detailed description of the analysis of assay results (see for example, page 38, line 29, to page 45, line 18, of the instant application) are the triangular geometric substructures recited in claim 1.

In another particular, the Examiner has stated that claim 1 introduces new matter by addressing "triangle space defining all possible 3-point pharmacophores,... wherein said 3-point pharmacophore represents a set of three binding points on a molecule to which a gauge may bind", as the specification does not address a triangle space as defined by possible 3-point pharmacophores.

As discussed hereinabove, "triangle space" is a mathematical tool for defining all possible 3-point pharmacophores (within a specified range of parameters), so as to precisely define what constitutes, e.g., 50 % of all possible 3-point pharmacophores. The term "triangle space" is used throughout the instant application, as are similar terms (e.g., "space", "measurement space", "configuration space", etc.), and Applicant strongly believes that it would be apparent to one of ordinary skill in the art that the description of "triangle space" in the claim language as defining all possible 3-point pharmacophores is entirely consistent with the usage of the term throughout the application. See for example, page 37, lines 11-14, which describes spanning of triangle space as the ability to bind to each triangular arrangement of binding points (i.e., 3-point pharmacophore).

See also, for example, page 19, lines 10-11, and page 21, lines 19-21, in which the term "configuration space" is used to define configurations of binding points. As would be apparent to one of skill in the art, "triangle space" refers to a configuration space for defining triangular configurations of binding points (e.g., 3-point pharmacophores).

35 U.S.C. § 103(a) Rejections

The Examiner has stated that claims 1-4, 26, 29-33, 36, 41-46, 155, 156, 158, 159 and 161 are rejected under 35 U.S.C. § 103(a) as obvious over Fejzo et al. in view

of Pickett et al. and also in view of Mason et al. The Examiner's rejection is respectfully traversed. Claims 5, 155 and 156 have now been canceled.

Specifically, the Examiner has stated that Fejzo et al. teaches a method of obtaining information about a chemically active area of a target molecule, comprising providing a set of diverse small molecules, assaying interaction of the gauges with the target, and analyzing the assay results to obtain information about the chemically active area. The Examiner has further stated that characterization of the space in which assaying occurs as "triangle space" does not affect patentability, as a solution remains the same solution even if it is addressed as "triangle space".

The Examiner has further stated that although Fejzo et al. does not teach that gauges can be described as comprising at least one set of three binding points in a substantially rigid triangular configuration and having at least one triangular geometric substructure defined by a triplet of distances and by a triplet of binding point types, Mason et al. and Pickett et al. teach that pharmacophores can be described in terms of their geometrical characteristics (e.g., their 3-point or 4-point descriptors), and that Pickett et al. teaches 3-point descriptors for pharmacophores using a 3D distance space with three point combinations of pharmacophoric groups, such that each pharmacophore can be addressed as the instantly claimed gauge.

Claims 5, 6, 8, 9, 14, 15, 24, 25, 34, 35, 40, 47-49, 54-56, 162 and 163 have not been rejected as obvious over Fejzo et al. in view of Pickett et al. and Mason et al.

As discussed hereinabove, claim 1 has been amended so as to recite limitations previously recited in claim 5.

As claim 5 has not been rejected as obvious, Applicant believes that the amendments to claim 1 render moot the Examiner's rejection over Fejzo et al. in view of Pickett et al. and Mason et al.

Notwithstanding the above, Applicant wishes to point out the many differences between the claimed subject matter and the teachings of the cited art.

As discussed in detail hereinbelow, Applicant contends that:

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a) the cited art clearly fails to teach selection of a plurality of gauges as recited in claim 1;

b) the cited art clearly fails to teach analysis of assay results as recited in claim 1; and

c) the techniques described by Pickett et al. and Mason et al. cannot be applied to the method described by Fejzo et al.

a) Gauges

The Examiner has stated that Fejzo et al. teaches small molecules corresponding to the gauges recited in the instant application.

Claim 1 recites a selection of a plurality of gauges so as to include at least six gauges capable of binding to each 3-point pharmacophore defined by at least 50% of a triangle space (hereinafter referred to as "spanning") which defines all possible triangular 3-point pharmacophores with distances in a range of 2-12 angstrom and with acid, base, hydrophobic, hydrogen-bond donor, hydrogen-bond acceptor and aromatic as possible binding point types at the vertices.

Such a selection comprises selecting gauges which bind to different 3-point pharmacophores than do previously selected gauges, in order to generate the structural diversity (e.g., diversity of triangle dimensions and diversity of binding point types) necessary for spanning at least 50% of the recited triangle space, as well as selecting sufficient additional gauges to provide the recited six gauges per 3-point pharmacophore.

It would be apparent to one of skill in the art that Fejzo et al. does not even remotely suggest such a selection of gauges.

Indeed, Fejzo et al. teaches away from the claimed invention by teaching the desirability of selecting a small number of compounds, i.e., 120 compounds or less (see page 757, first paragraph, as well as the paragraph bridging pages 760 and 761, of Fejzo et al.). Selection of such a small number of selected compounds provides

little, if any, information regarding a structure of target molecule. Furthermore, Fejzo et al. neither teaches nor suggests how information obtained can be usefully used with a model, for example, to identify configurations of binding points in the target molecule.

A ***single*** set of distances of a triangle allows the arrangement of the 6 possible binding types on the three triangle vertices in many different combinations, resulting in $6^3 = 216$ possible triangles. Moreover, spanning, as defined in claim 1, requires more than one gauge for each possible triangle.

Although gauges may comprise several triangular configurations, and a binding point may fit more than one binding type (e.g., hydrophobic and aromatic), it is clear that the 120 compounds taught by Fejzo et al. are far from being able to span ***all*** possible combinations of three triangle distances to an average extent of 50%.

Moreover, Fejzo et al. teaches that selection of small molecules is advantageous (see for example, page 756, Results section, first sentence, in Fejzo et al.).

Of the frameworks taught by Fejzo et al. (see Figure 1 therein), those which are rigid are almost exclusively comprise a single aromatic rings or a fused bicyclic system. The possible distances allowed by molecules with such frameworks range only up to approximately 7 angstrom (e.g., the farthermost carbon atoms on naphthalene, an exemplary bicyclic compound taught by Fejzo et al., are approximately 5 angstrom apart), which represents only half of the range of 2-12 angstrom represented in the triangle space defined hereinabove.

Triangles wherein all three distances are in the lower half of the allowed range are limited to approximately $(1/2)^3 = 1/8$ of triangle space. Hence, the compounds of Fejzo et al. are limited to a very small portion of triangle space, and therefore can contribute very little to spanning the required 50% of triangle space.

In sharp contrast to Fejzo et al., selection of a plurality of gauges according to the claimed invention would include many gauges with larger rigid scaffolds (e.g.,

tricyclic and tetracyclic compounds) so as to provide triangle distances throughout the range of 2-12 angstrom (see for example, pages 83-86, Section 14.3, of the instant application).

Moreover, Fejzo et al. teaches neither selection for substantially rigid compounds comprising at least one set of binding points in a substantially rigid triangular configuration.

Thus, the compounds selected by Fejzo et al. include numerous non-rigid compounds, and have few, if any, binding points attached thereto which are suitable for chemically binding to an acid, base, hydrophobic, hydrogen-bond donors, hydrogen-bond acceptors or aromatic. Few combinations of side chains are added to the frameworks used by Fejzo et al., as only 132 compounds were generated from 32 frameworks (see page 757, first paragraph, and Figure 1, of Fejzo et al.). Thus, Fejzo et al. preferentially selects for compounds which fail to comprise a single substantially rigid triangular configuration suitable for binding a 3-point pharmacophore.

Thus, the Fejzo et al. fails to teach or suggest selection of gauges in order to provide a high level of diversity required to obtain structural information according to embodiments of the claimed invention.

b) Analysis of assay results

Claim 1 recites:

"identifying a plurality of spatially and chemically specific configurations of binding points in said chemically active area of said target molecule using a computational model in which said assay results represent interactions between configurations of binding points in said chemically active area and triangular geometric substructures, each triangular geometric substructure representing a set of three binding points of a gauge and being defined by a triplet of distances that form a triangle and by a triplet of chemical binding point types for the triangle vertices"

As argued in Applicant's response filed May 22, 2009, Fejzo et al. neither teaches nor suggests using triangular geometric substructures in analysis of assay results. Indeed, Fejzo et al. does not teach or suggest any type of analysis of assay results, as the only information provided by the method of Fejzo et al. is which compounds in the library bind to the target. Consequently, no structural information is obtained.

The Examiner has not disputed Applicant's above characterization of Fejzo et al. For example, the Examiner has stated that "Fejzo et al. do not teach all the characteristics of testing "gauges" as instantly claimed, i.e., that the gauges can be described as...having at least one triangular geometric substructure etc.". Instead, the Examiner has stated that Mason et al. and Pickett et al. teach that pharmacophores can be described in terms of their geometrical characteristics.

Mason et al. teaches a pure *in silico* method of analyzing *known structures* of compounds and protein sites, in order to find common 4-point pharmacophores. Mason et al. does not in any way relate to either analysis of assay results or to obtaining new information regarding the structure of a target molecule, let alone to identifying configurations of binding points in the target.

Thus, Mason et al. clearly fails to teach identifying a plurality of spatially and chemically specific configurations of binding points in a target molecule.

Moreover, Mason et al. clearly fails to teach using a computational model in which *in vitro* assay results are used to represent interactions between configurations of binding points in a target molecule and triangular geometric substructures.

Moreover, Mason et al. does not teach analysis based on 3-point pharmacophores, and in fact teaches away from such analysis by stating that the increased information present in 4-point pharmacophoric descriptions is normally needed (see Section 3.1, first paragraph, of Mason et al.). Hence, Mason et al. would not motivate one of skill in the art to use a model based on *triangular* geometric substructures.

Pickett et al. teaches a pure *in silico* method of partitioning *known structures* of compounds in terms of three-center pharmacophores expressed by the compounds (see, for example, Section 1.1 of Pickett et al.). Pickett et al. does not in any way relate to either analysis of assay results or to obtaining new information regarding the structure of a target molecule, let alone to identifying configurations of binding points in the target. Indeed, Pickett et al. does not appear to discuss any sort of target molecules at all.

Thus, Pickett et al. clearly fails to teach identifying a plurality of spatially and chemically specific configurations of binding points in a target molecule.

Moreover, Pickett et al. clearly fails to teach using a computational model in which assay results represent interactions between configurations of binding points in a target molecule and triangular geometric substructures.

Thus, Fejzo et al., Pickett et al. and Mason et al., either alone or in combination, fail to teach or even remotely suggest identifying a plurality of spatially and chemically specific configurations of binding points in a chemically active area of a target molecule using a computational model in which *in vitro* assay results represent interactions between configurations of binding points in the chemically active area and triangular geometric substructures, as recited in claim 1.

c) Application of techniques described by Pickett et al. and Mason et al. to the method described by Fejzo et al.

The Examiner has stated that the combination of Pickett et al. and Fejzo et al. is applying a known technique of characterizing pharmacophores to a known method describing ligand-target molecule interaction.

It is unclear to Applicant what the Examiner's position is regarding Mason et al., hence it is assumed herein that Mason et al. is equivalent to Pickett et al.

As discussed hereinabove, Fejzo et al. describes a method comprising performing binding assays for a small number of compounds, and finding a small

number of compounds (e.g., 5-6 % of a library of 100-300 compounds) which bind weakly to a target and can therefore potentially serve as leads for drug design (see for example, Abstract and page 763, second paragraph, therein). Fejzo et al. teaches the use of particular NMR methods in order to allow detection of such weak binding (see for example, paragraph bridging pages 764 and 765, therein).

Identifying a small number of weakly binding compounds does not provide sufficient information regarding the structure of the target to be of any real use in identifying configurations of binding points in the target.

Furthermore, the method of Fejzo et al. is unsuitable for obtaining structural information (e.g., configurations of binding points in the target) from binding assay results, as the number of compounds used in the method of Fejzo et al. is too small and lacking in diversity to provide any significant information beyond identifying several weakly binding compounds. Thus, Fejzo et al. neither teaches nor suggests that the method described therein is capable of providing information regarding the structure of a target molecule (see for example, page 767, "Significance" section, of Fejzo et al.).

In addition, as discussed hereinabove, the number of compounds used by Fejzo et al. is clearly too small and lacking in diversity to enable identification of a plurality of configurations of binding points in a target in accordance with embodiments of the claimed invention.

In view of the above, one of ordinary skill in the art would not attempt to use the method of Fejzo et al. in order to characterize the structure of a target, either by identifying a plurality of configurations of binding points in the target, or by any other means.

As further discussed hereinabove, Pickett et al. and Mason et al. teach pure *in silico* methods for analyzing known structures of molecules. Pickett et al. and Mason et al. do not describe any technique for analyzing the structure of a molecule when the structure is unknown.

Consequently, one of ordinary skill in the art would not use the methods taught by Pickett et al. or Mason et al. to analyze the structure of a target molecule unless the structure has already been characterized using a different method.

Thus, the techniques of Pickett et al. and Mason et al. require known molecular structures as an input, and the method of Fejzo et al. neither intends to provide nor is capable of providing any structural information (let alone a complete molecular structure) as an output. Consequently, the techniques of Pickett et al. and Mason et al. are fundamentally incapable of being applied to the method of Fejzo et al., as the assays taught by Fejzo et al. do not enable analysis of the results by the techniques of either Pickett et al. or Mason et al.

In sharp contrast, claim 1 recites a method comprising selection of gauges, *in vitro* assaying and analysis of the assay results, in which the gauges are specifically selected so as to enable obtaining structural information by analysis of the assay results.

In view of the above, Applicant believes that the claims are not obvious over Fejzo et al. in view of Pickett et al. and/or Mason et al., and are therefore allowable.

Additional Amendments

Claims 2 and 6 have been amended in order to improve the clarity thereof, and so that the language thereof will better accord with the language of amended claim 1. Applicant contends that the aforementioned amendments to claims 2 and 6 are cosmetic and do not affect the scope of the claims.

Thus, claim 2 has been amended so as to recite:

"...wherein said additional gauges are selected such that for a portion of triangle space comprising 50 % of a triangle space that defines all possible 3-point pharmacophores defined by a triplet of distances that form a triangle, each distance being in a range of 4-8 angstrom, and by a triplet of chemical binding point types for

the triangle vertices, each chemical binding point type being selected from the group consisting of acid, base, hydrophobic, hydrogen-bond donor, hydrogen-bond acceptor, and aromatic, said plurality of gauges is selected so as to comprise at least six gauges with a substantially rigid triangular configuration of binding points capable of chemically binding to each 3-point pharmacophore corresponding to a point in said portion of triangle space."

Claim 6 has been amended so as to recite "said spatially and chemically specific configurations" instead of "said configurations".

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In view of the above amendments and remarks it is respectfully submitted that claims 1-4, 6-25, 29-57, 102, 103, 157-159 and 161-163 are now in condition for allowance. A prompt notice of allowance is respectfully and earnestly solicited.

Respectfully submitted,

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Date: December 22, 2009

Enclosures:

- Petition for Extension (2 Months)
- Request for Continued Examination (RCE)